CONDITIONAL PETITION FOR EXTENSION OF TIME

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefor. The Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

REMARKS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

New claim 11 is added, which has the scope of claim 3 except that inhalative application has been deleted without prejudice. Applicants do not believe new claim 11 introduces any new matter. An early notice to that effect is earnestly solicited.

New claim 11 should be free of the prior art rejections, which are all based on modifying a voltage delivering device to deliver a chemical inhalatively.

Claims 1-4 and 7-10 were rejected under 35 USC § 103(a) as being obvious over Christopherson et al. ("Christopherson"), US 5,944,680, in view of Winokur et al. ("Winokur"), US 5,968,932, in view of Higenbottam et al. ("Higenbottam"), WO 00/01434, in view of Willmann et al. ("Willmann"), *Biosilico, 1:* 121-124 (2003). In response, Applicants respectfully submit that the combination of Christopherson, Winokur, Higenbottam and Willmann fails to make out a *prima facie* case of the obviousness of any of the rejected claims. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

In order to make out a *prima facie* case of obviousness based on a combination of references, an examiner must provide "some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *See, In re Kahn,* 441 F.3d 977, 988 (Fed. Cir. 2006), *cited with approval in KSR Int'l Co. v. Teleflex, Inc.,* 550 U.S. 398, 419

(2007). In response, an applicant can attack the proposed combination by articulating persuasive reason(s) that the rational underpinning is missing and that persons skilled in the art would not, in fact, have combined the prior art teachings in the manner the examiner surmises or that combination in the manner the examiner advocates does not, in fact, achieve the claimed invention.

In the response to arguments, the Examiner says at the top of page 10 of the final rejection that Applicants' arguments are not persuasive because they do not take into account all of the references in the rejection. Applicants respectfully disagree with this assessment and respectfully submit that the Examiner has mischaracterized the references and that it would have been clear to any person skilled in the art that the references cannot be combined in the manner the Examiner supposes.

According to the Examiner:

> "While Winokur et al. teaches ***inhalation*** of Montirelin for sleep apnea, and while Christopherson et al. teaches automated dosaging of voltages in the ***respiratory tract*** to also control sleep apnea; the references of Higgenbottam et al. (not directly addressed in the Remarks) teaches an electronic and automated inhaler that administers chemicals to the ***respiratory tract.*** Consequently, the combination of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. make obvious two alternative forms of delivering dosages to the ***trachea:*** the first method is by delivering dosages of voltages to the trachea; the second method is electronically delivering Montirelin to the ***respiratory tract*** through an automated inhaler. There would have been a reasonable expectation of success in combining Christopherson et

al., Winokur et al., Higenbottam et al., and Willmann et al. because the combination of references analogously pertains to understanding the delivery of drugs or voltages to the ***respiratory tract*** to better comprehend or simulate sleep apnea. [Emphasis added]."

The Examiner, in attempting to tie the various references together, indicates they have in common delivery "to the respiratory tract." However, this is misleading, as the respective devices have very different function and goals, which makes impossible combining their teachings in any meaningful way as to achieve the present invention.

The Examiner sees Christopherson as teaching the present invention save for the use of a medicament and the use of simulations based on physiology-based pharmacokinetic profiling. Winokur is relied on to teach "inhalation" of Montirelin, but is said to lack a teaching of automated administration. Higenbottam is relied on to teach the structure and function of an automated inhaler that administers a chemical to "the trachea and lungs" and to provide motivation to combine Christopherson and Winokur Willmann is relied on to teach the use of simulations based on physiology-based pharmacokinetic profiling.

According to the Examiner, persons skilled in the art would have found it obvious to modify Christopherson's implanted device that applies voltages and to adapt such device to the administration of Montirelin as taught by Winokur. According to the Examiner such person would have been motivated in this direction *by Higenbottam's success* in automated dosing of chemicals to the trachea and lungs. According to the Examiner, such a person would further have been motivated to use Willmann's simulations based on physiology-based pharmacokinetic profiling in order to optimize dosing under optimal conditions.

All of the foregoing is in the context of treatment of sleep apnea and Applicants respectfully submit that this is where the Examiner's entire premise breaks down.

Christopherson teaches implantation of his device to affect the hypoglossal nerve for stimulation of the genioglossus muscle of the upper airway. See column 7, lines 56-57. Consequently, Christopherson is not concerned with the respiratory tract generally, but, rather, the upper airway. Indeed, see the very high placement of the airway obstruction **17** in Christopherson's Figure 3. Sleep apnea is characterized by obstruction in the upper airway, not the lungs.

Winokur teaches that Montirelin is administered as a bolus injection and, if parenterally, possibly by ***intranasal*** inhalation. There is, thus, in Winokur no teaching or suggestion that Montirelin is administered over time, for example, at different points of time during the night, consequently, there is nothing in Winokur that would have motivated persons skilled in the art to modify Christopherson in a manner to administer Montirelin over time or, therefore, with a program that optimizes the dosing schedule. Further, persons skilled in the art would not have been motivated to implant Christopherson's modified device now administering Montirelin ***intranasally.*** From a practical standpoint, this makes no sense and persons skilled in the art would not have done it.

While the Examiner is correct that Higenbottam relates to inhalers, such are not adapted to deliver intranasally, or even to the patient's trachea and lungs generally, as the Examiner mischaracterizes Higenbottam's teachings. Rather, Higenbottam's inhalers are specially designed, but, rather, to the deepest parts of the lungs. Indeed, see the next to last paragraph on page 13 of Higenbottam: The device is designed to deliver a bolus dose deep within the

respiratory tract in such a way that "the bolus remains as an entity and does not disperse as it progresses (and so reaches ***the deepest part of the lungs*** as a concentrated burst of medicament with the full therapeutic effect required)." Consequently, contrary to the Examiner's characterization of Higenbottam's teachings, Higenbottam does not deliver intranasally, which is where Winokur teaches Montirelin administration to treat sleep apnea, nor does Hignbottam deliver to the upper respiratory track or even the trachea, but, instead, delivers deep within the lungs (where the record does not reflect sleep apnea has a basis.) Consequently, the Examiner's statement that Higenbottam shows success in automating dosing of chemicals to the trachea and lungs is simply inaccurate and incorrect. Accordingly, the Examiner is likewise incorrect that persons skilled in the art, motivated by these nonexistent Higenbottam teachings, would have been further motivated to modify Christopherson's implanted device that applies voltages to the administration of Montirelin as taught by Winokur.

Nothing in the combination of Christopherson, Winokur and Higenbottam teaches or suggests implanted delivery of bolus Montirelin intranasally with a reasonable expectation of success. Consequently, persons skilled in the art would not, in fact, have been motivated to proceed in the manner the Examiner proposes. Even if Willmann teaches simulations based on physiology-based pharmacokinetic profiling, the failure of the combination of Christopherson, Winokur and Higenbottam to motivate in the direction the Examiner surmised means that the combination of Christopherson, Winokur, Higenbottam and Willmann is still deficient, failing to teach the present invention. No reason is given and none is apparent why a person skilled in the art should desire to apply physiology-based pharmacokinetic profiling in the case of bolus Montirelin.

In short, the requisite rational underpinning to this rejection is not present on this record. Therefore, the Examiner must reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Claim 5 was rejected under 35 USC § 103(a) as being obvious over Christopherson in view of Winokur in view of Higenbottam in view of Willmann, and further in view of Sugita et al. ("Sugita"), US 2003/0175350. In response, Applicants respectfully submit that this rejection was dependent upon the combination of Christopherson, Winokur, Higenbottam and Willmann rendering *prima facie* the broad aspects of the present invention as embodied in main claim 1. Since it has been shown above that this is not, in fact, the case, Applicants respectfully submit that this rejection also should be reconsidered and withdrawn. Indeed, nothing in Sugita overcomes the above-noted defects in Christopherson, Winokur, Higenbottam and Willmann. Accordingly, the combination of Christopherson, Winokur, Higenbottam, Willmann and Sugita likewise fails to make out a *prima facie* case of the obviousness of claim 5.

Claim 6 was rejected under 35 USC § 103(a) as being obvious over Christopherson in view of Winokur in view of Higenbottam in view of Willmann, and further in view of the definition of "numerical modeling" in *The Dictionary of Physical Geography* (2000). In response, Applicants respectfully submit that this rejection was dependent upon the combination of Christopherson, Winokur, Higenbottam and Willmann rendering *prima facie* the broad aspects of the present invention as embodied in main claim 1. Since it has been shown above that this is not, in fact, the case, Applicants respectfully submit that this rejection also should be reconsidered and withdrawn. Indeed, nothing in *The Dictionary of Physical Geography* overcomes the above-noted defects in Christopherson, Winokur, Higenbottam and Willmann.

Accordingly, the combination of Christopherson, Winokur, Higenbottam, Willmann and *The Dictionary of Physical Geography* likewise fails to make out a *prima facie* case of the obviousness of claim 6.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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